

### AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the following Listing of Claims.

#### Listing of Claims:

1. (currently amended) An isolated polynucleotide encoding a variant human cytochrome P450 3A4 (~~CYP3A4~~) monooxygenase polypeptide or fragment thereof wherein the polynucleotide is selected from the group consisting of:
  - (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 90;
  - (b) a polynucleotide encoding a polypeptide ~~having~~ comprising the amino acid sequence of SEQ ID NO: 155;
  - (c) a polynucleotide encoding ~~an a~~ CYP3A4 polypeptide, wherein said polynucleotide comprises a sequence corresponding to SEQ ID NO: 90 and comprises a T at the position that corresponds to position 6 of SEQ ID NO: 90 ~~is having at a position corresponding to position 21867 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1)~~ a T,
  - (d) a polynucleotide encoding ~~an a~~ CYP3A4 polypeptide, wherein said polypeptide comprises a sequence corresponding to SEQ ID NO: 155, and comprises an amino acid substitution at the position that corresponds to position 21 of SEQ ID NO: 155 ~~at position 363 of the CYP3A4 polypeptide (Accession No: AF280107)~~; and
  - (e) a polynucleotide encoding ~~an a~~ CYP3A4 polypeptide, wherein said polypeptide comprises a sequence corresponding to SEQ ID NO: 155, and comprises an amino acid substitution of T to M at the position that corresponds to position 21 of SEQ ID NO: 155 ~~at position 363 of the CYP3A4 polypeptide (Accession No: AF280107)~~,wherein the polypeptide encoded by the polynucleotide is a variant human cytochrome P450 3A4 monooxygenase polypeptide or fragment thereof, wherein said polypeptide has testosterone or progesterone hydroxylase activity, and wherein said polypeptide has an impaired expression and impaired testosterone or progesterone hydroxylase enzymatic

activity compared to the corresponding wild type human cytochrome P450 3A4 monooxygenase CYP3A4-polypeptide.

2. (canceled).
3. (currently amended) The polynucleotide of claim 1, wherein the nucleotide substitution results in altered expression of the variant cytochrome P450 3A4 monooxygenase CYP3A4-gene compared to the corresponding wild type gene.
4. (previously presented) A vector comprising the polynucleotide of claim 1 or 3.
5. (previously presented) The vector of claim 4, wherein the polynucleotide is operatively linked to expression control sequences allowing expression in prokaryotic or eukaryotic cells.
6. (previously presented) An isolated host cell genetically engineered with the polynucleotide of claim 1 or 3 or the vector of claim 4 or 5.
7. (currently amended) A method for producing a molecular variant cytochrome P450 3A4 monooxygenase CYP3A4-polypeptide or fragment thereof comprising
  - (a) culturing the host cell of claim 6; and
  - (b) recovering said polypeptide or fragment from the culture.
8. (currently amended) A method for producing cells capable of expressing a molecular variant cytochrome P450 3A4 monooxygenase CYP3A4-gene comprising genetically engineering cells with the polynucleotide of claim 1 or 3 or the vector of claim 4 or 5.
- 9-11. (canceled).

12. (previously presented) An isolated nucleic acid molecule fully complementary to a polynucleotide of claim 1 or 3.
13. (previously presented) A vector comprising the nucleic acid molecule of claim 12.
- 14-36. (canceled).
37. (previously presented) A primer or probe consisting of an oligonucleotide of about 15 to 50 nucleotides in length and comprising a fragment of the polynucleotide of claim 1 or a fully complementary sequence thereof wherein said fragment comprises SEQ ID NO:90.
38. (canceled).
39. (previously presented) A composition comprising the polynucleotide of claim 1 or 3.
40. (previously presented) The composition of claim 39 which is a diagnostic or a pharmaceutical composition.